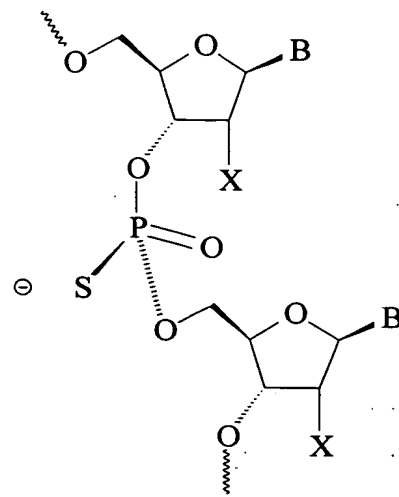


Rp isomer



Sp isomer

Figure 1

ISIS-4288 SHEET 1

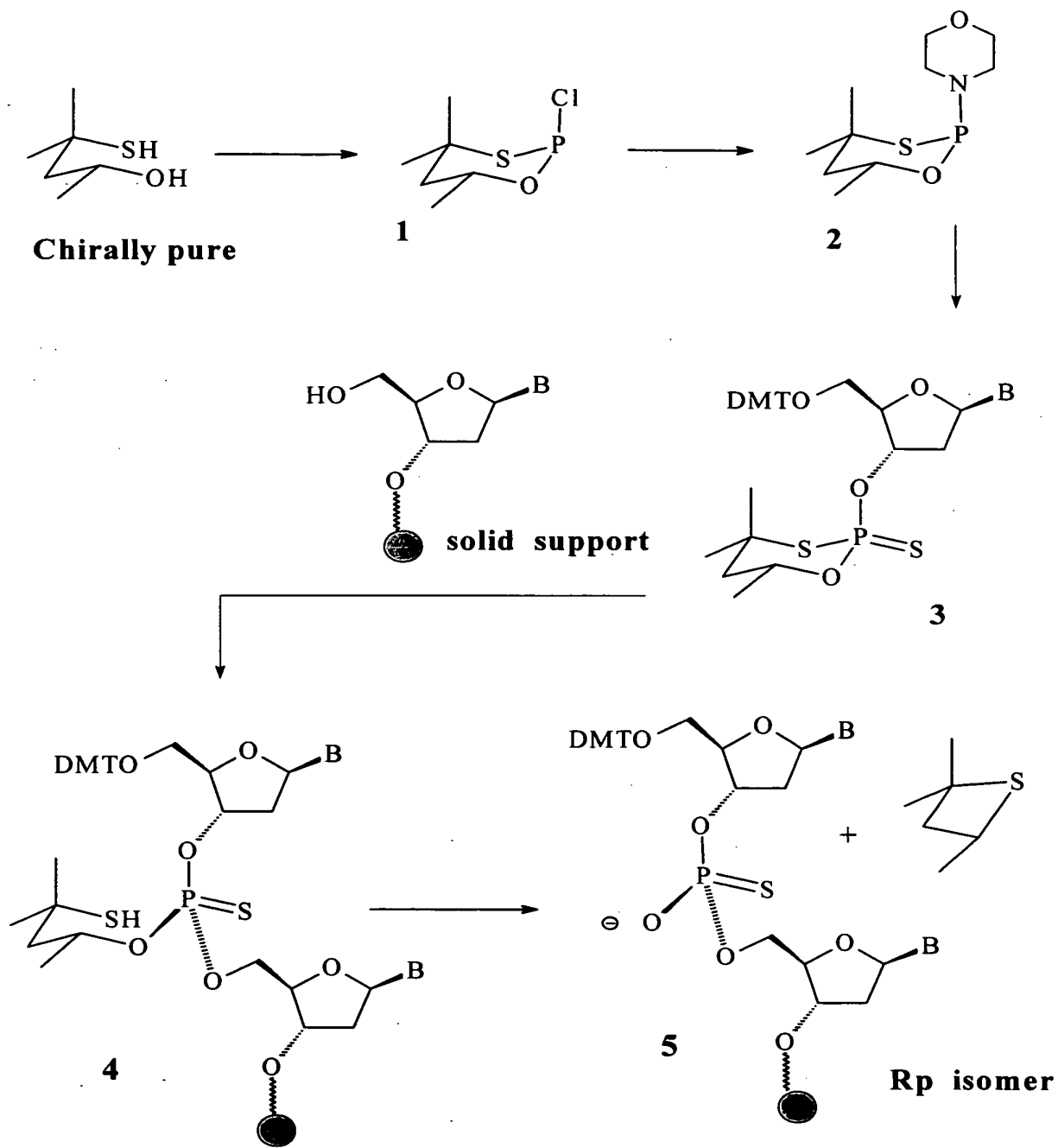


Figure 2

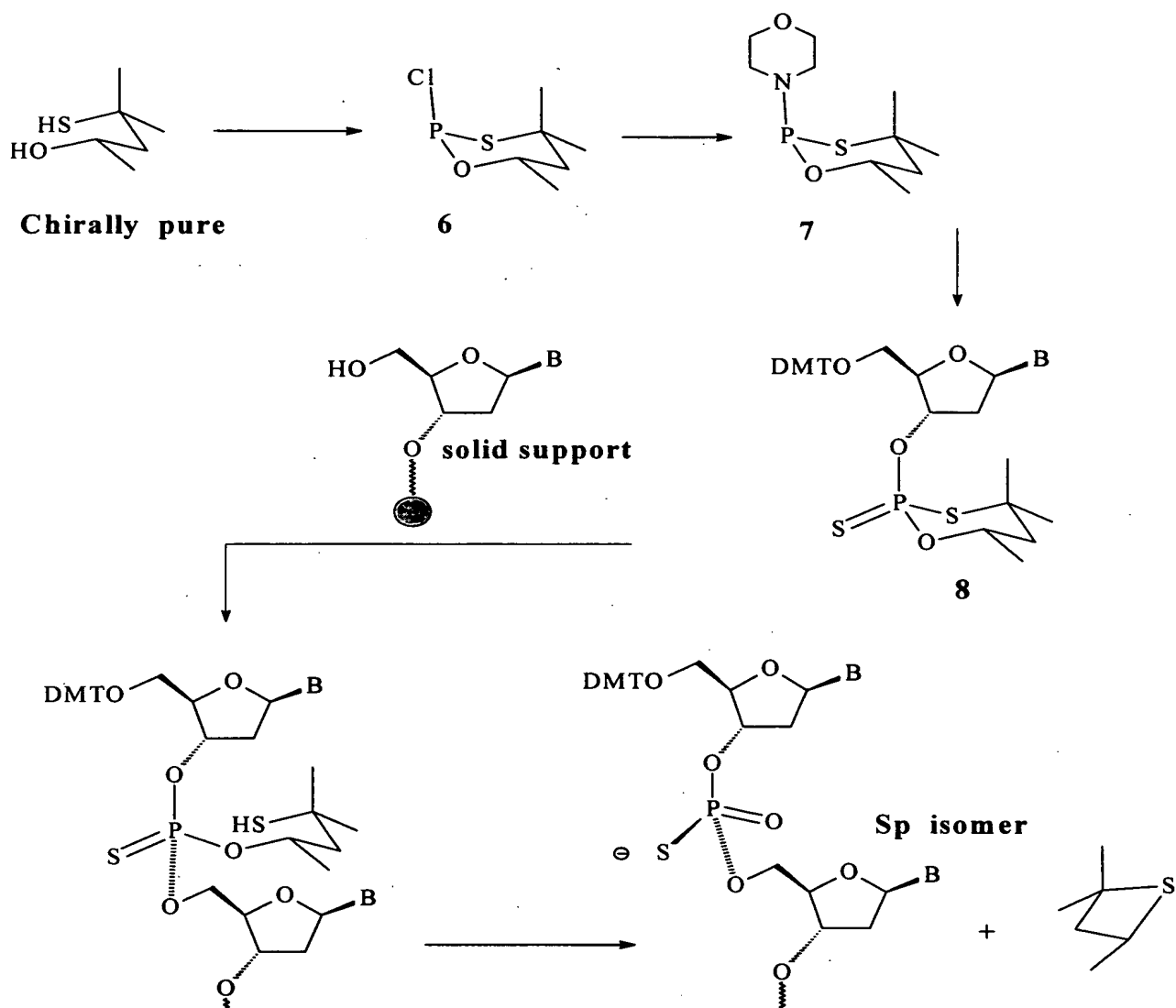


Figure 3

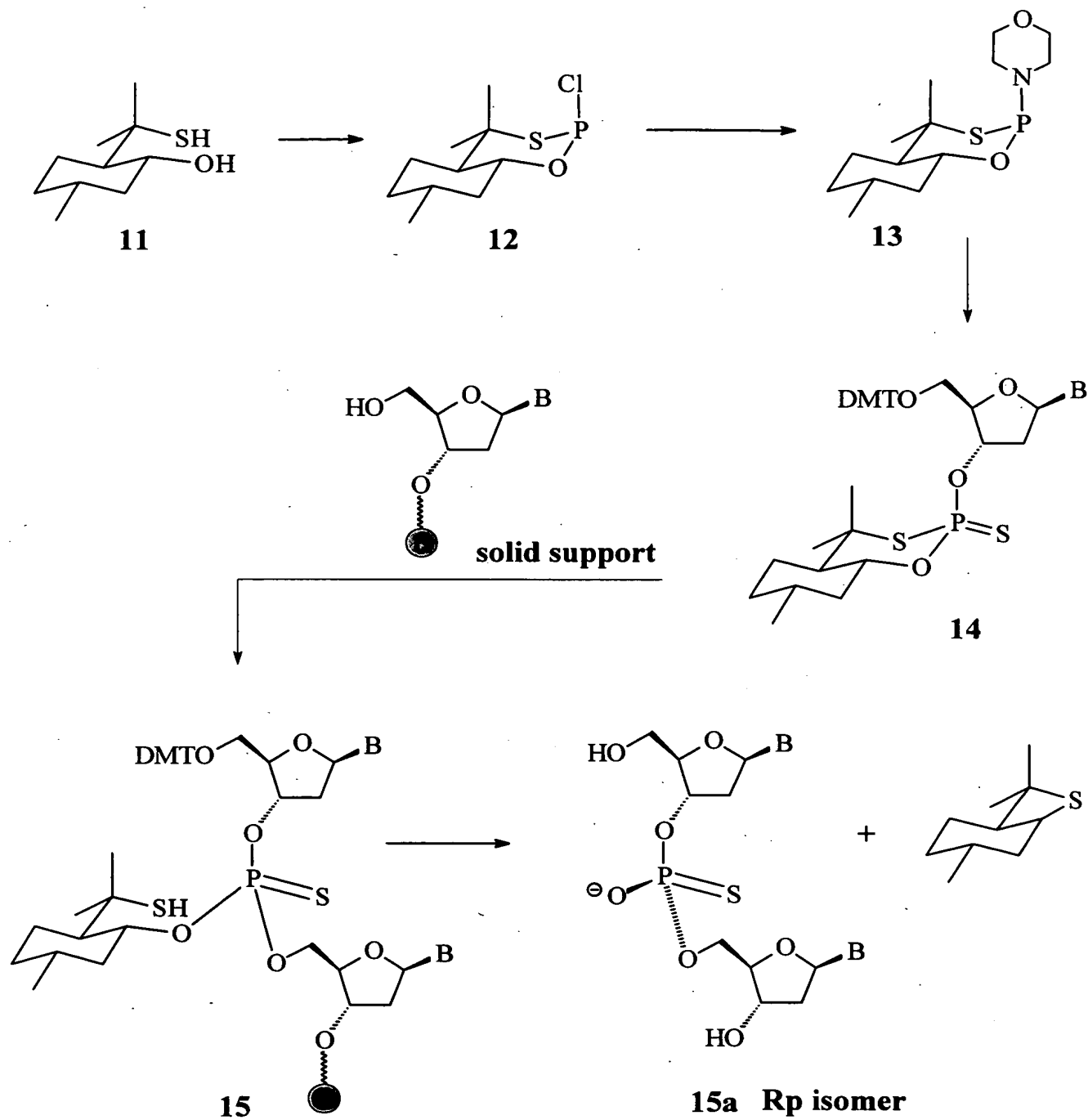


Figure 4

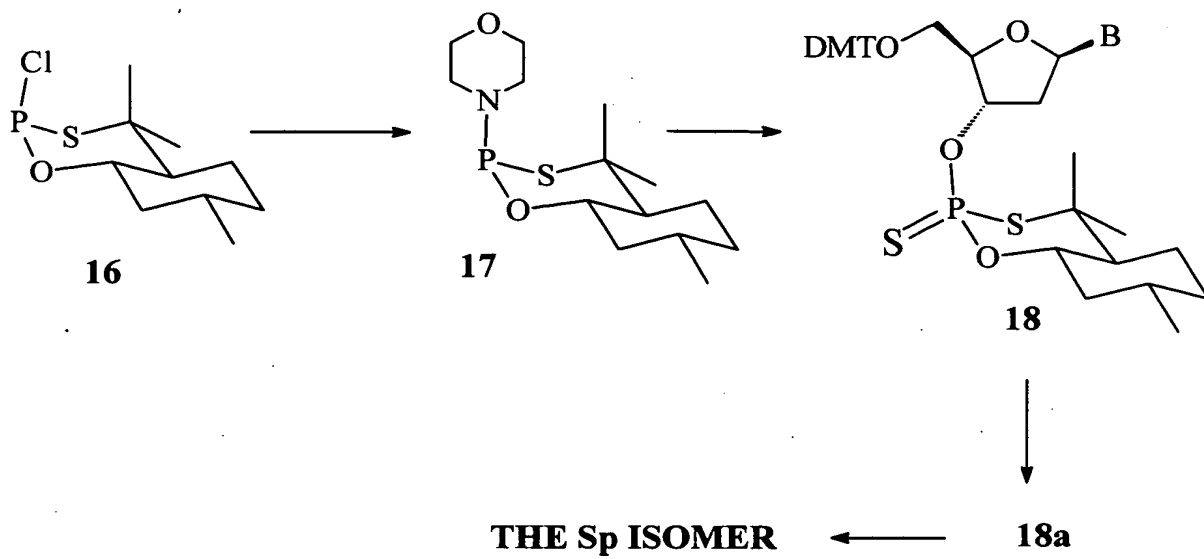


Figure 5

ISIS-4288 SHEET 5

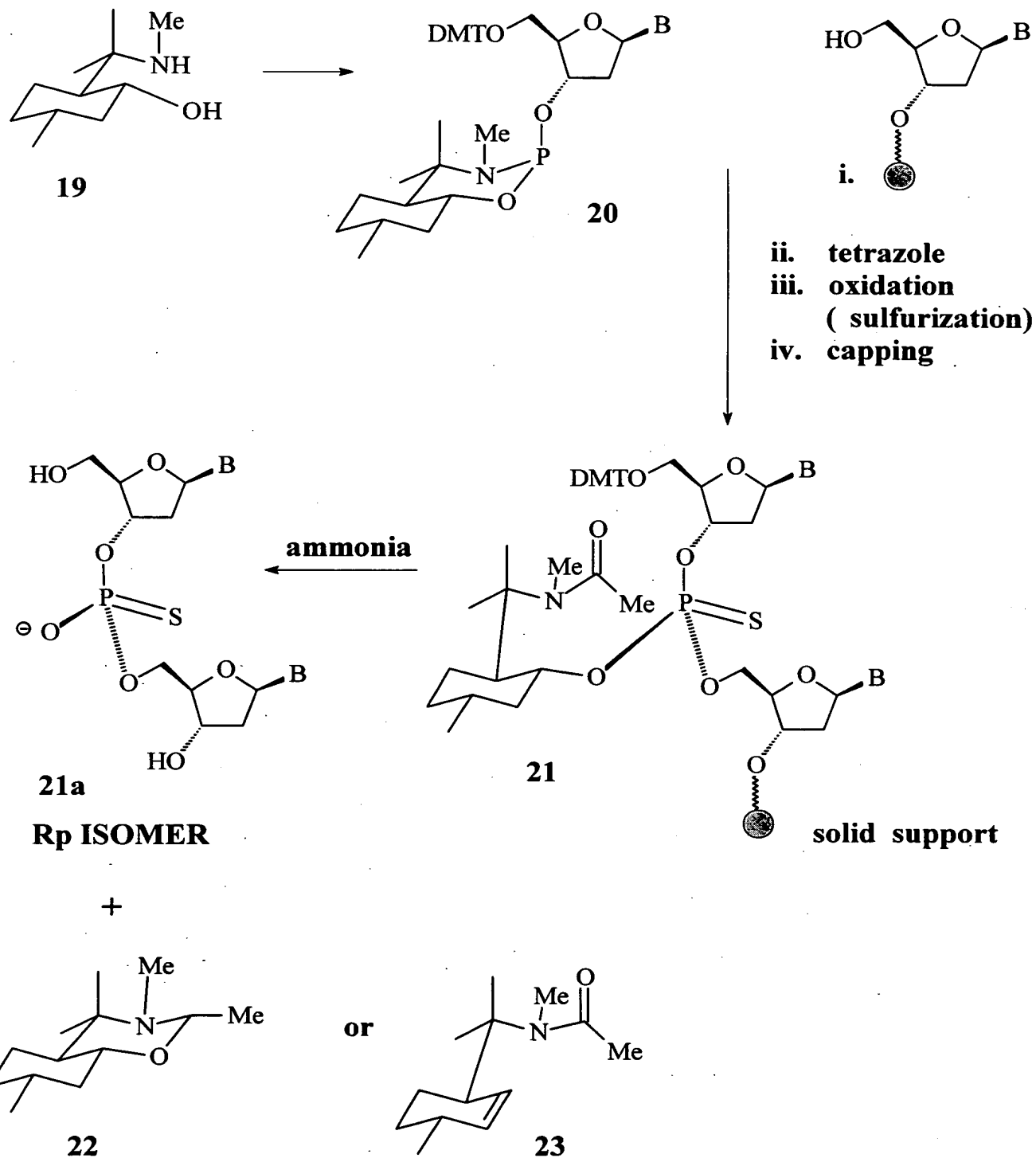


Figure 6

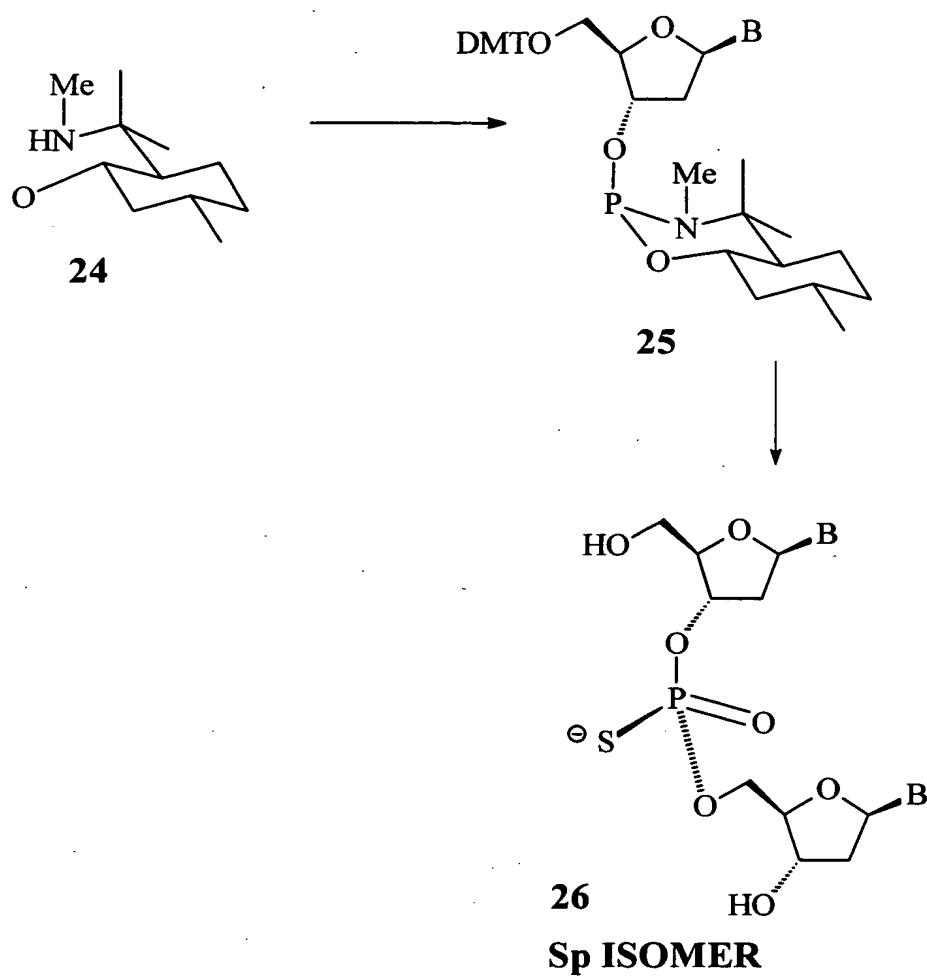
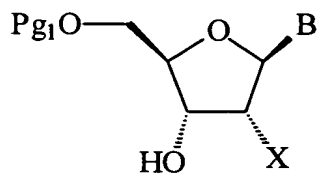


Figure 7

Building-Blocks: 5'-Pieces



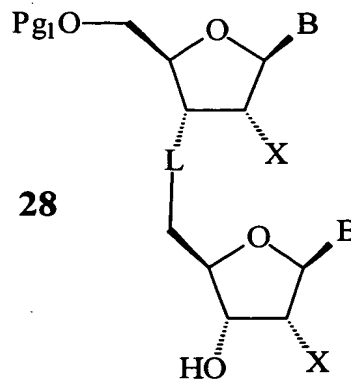
27

B = Base/Heterocycle

X = 2'-substituent group

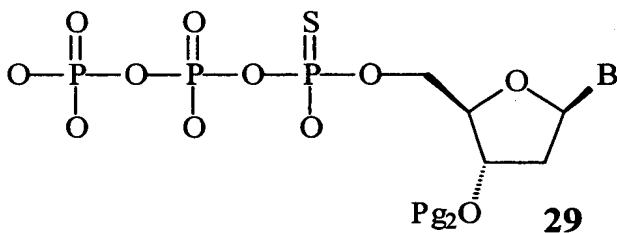
L = Linker, PS, dimer, trimer

Pg₁ = Protecting group

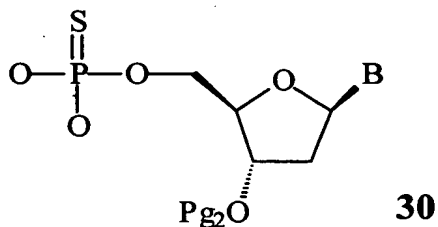


28

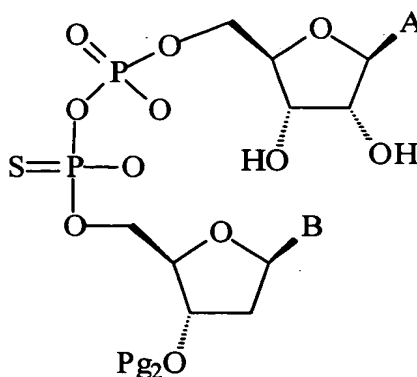
Building-Blocks: Pieces



29



30



31

Figure 8

Building-Blocks: 3'-Pieces

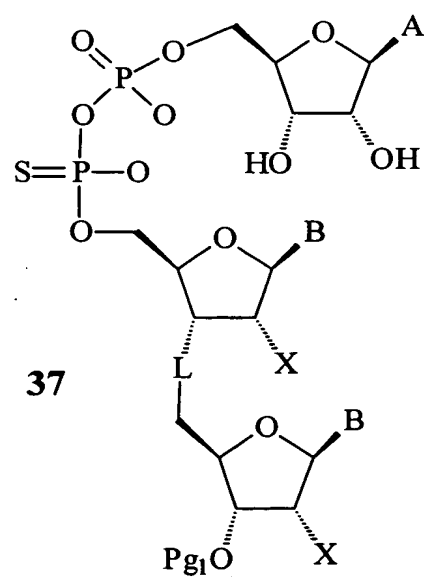
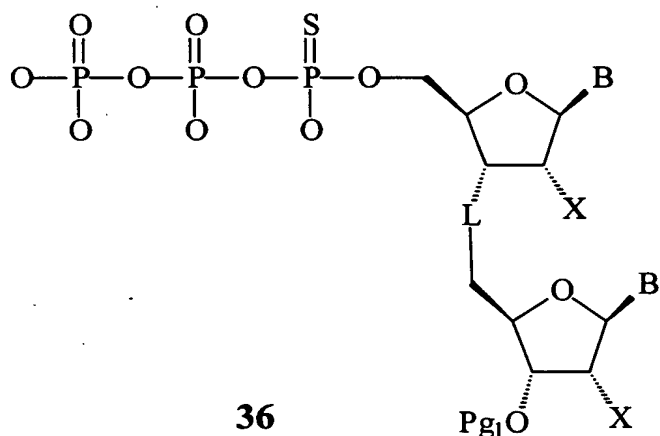
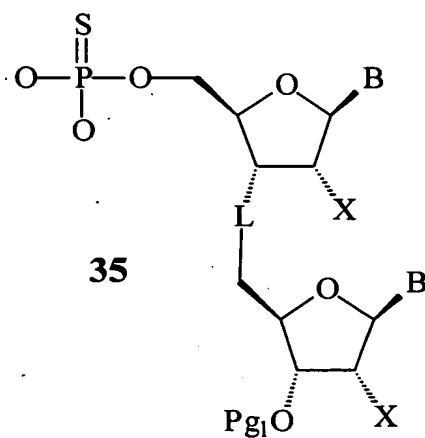
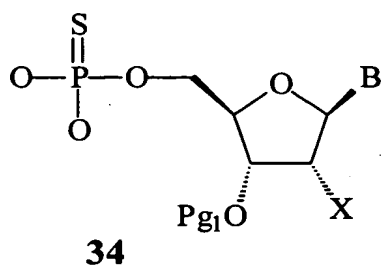
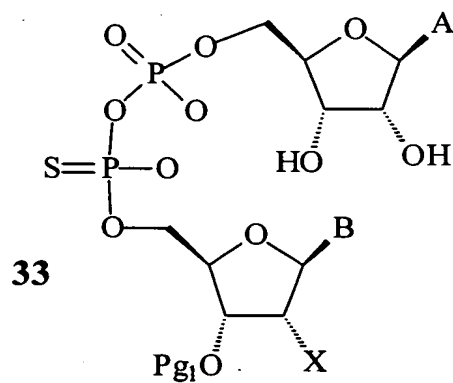
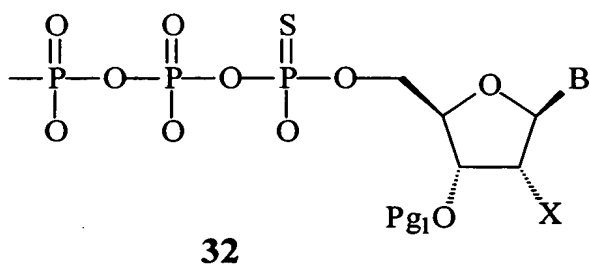
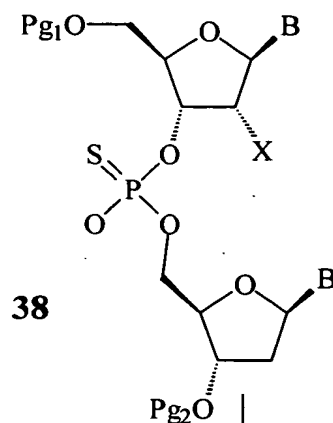


Figure 9

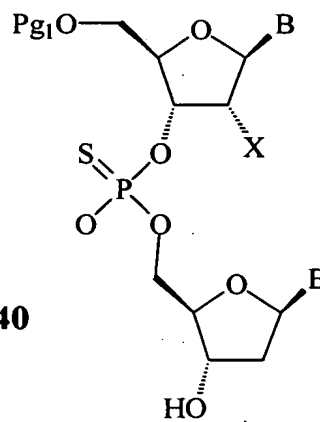
SHEET 9

Step 1: Coupling of 5'-Piece with Middle Block

27 + 29/30/31



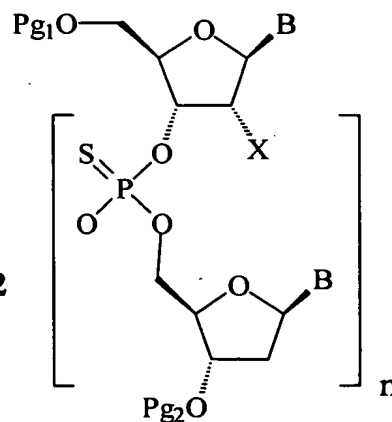
Step 2: Removal of Pg₂



39



Step 3: Repeat Coupling



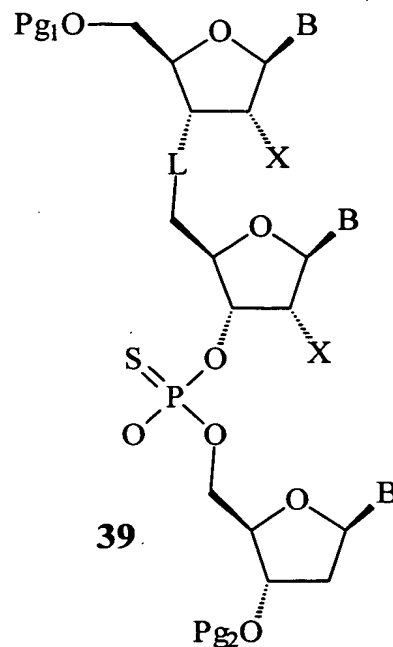
41



Figure 10

Step 1: Coupling of 5'-Piece with Middle Block

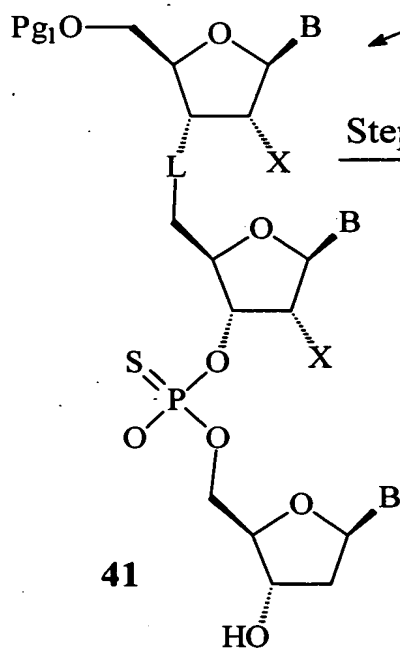
28 + 29/30/31



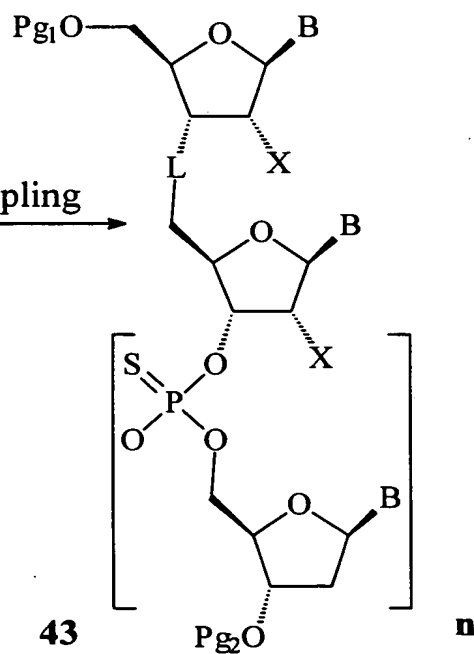
39



Step 2: Removal of Pg2



Step 3: Repeat Coupling



41



Figure 11

Step 4: Repeat Removal of Pg_2

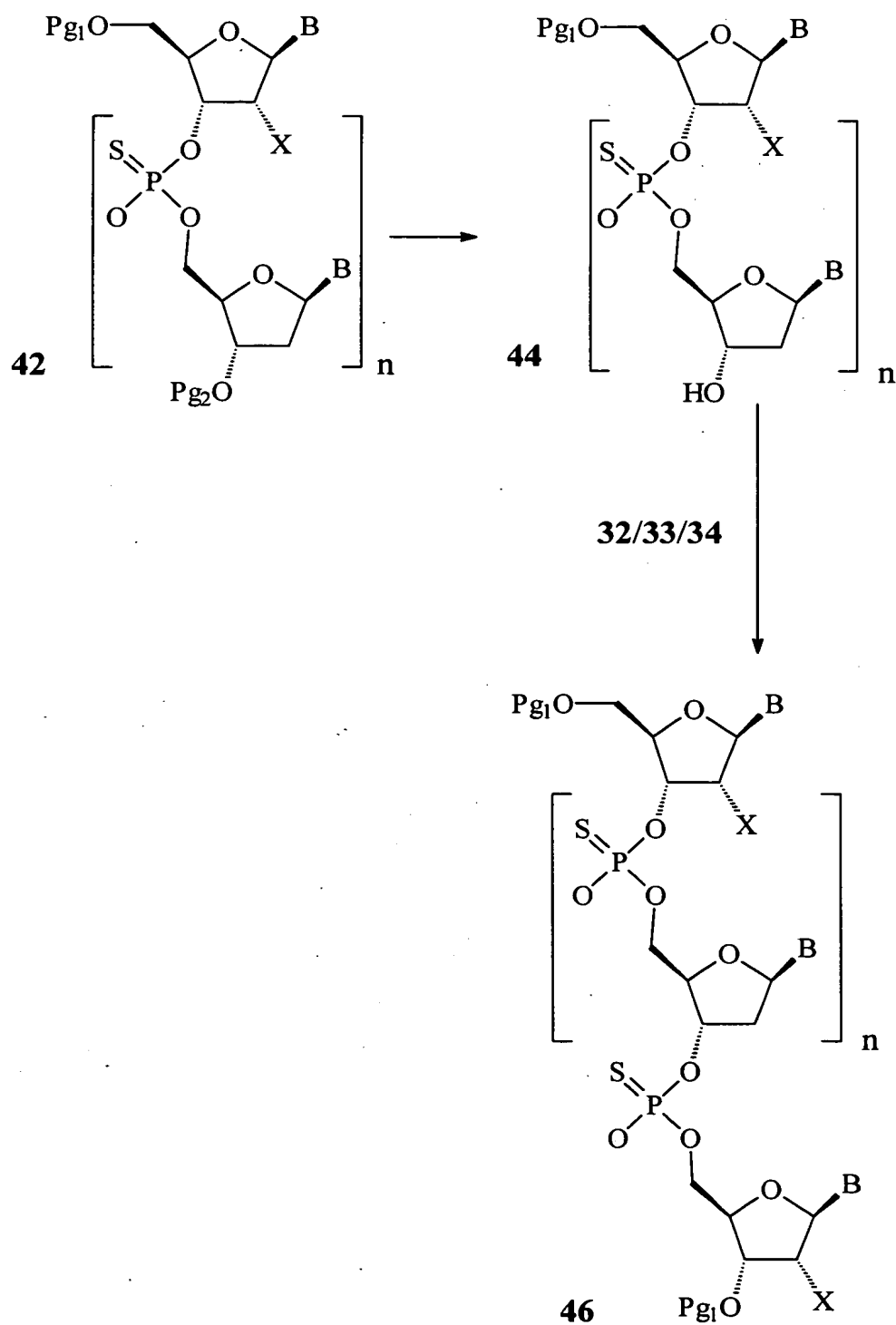


Figure 12

Step 5: Coupling with 3'-Pieces

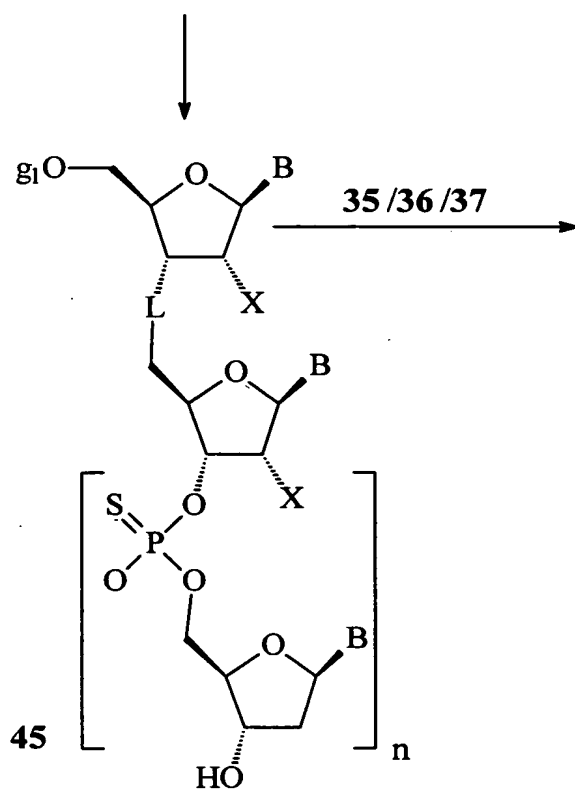
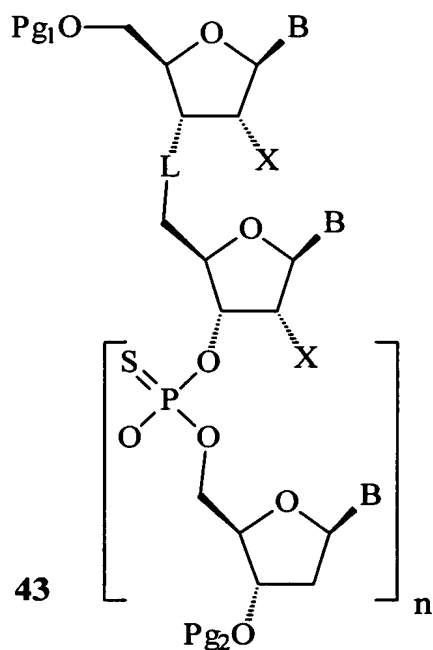


Figure 13

The image displays two chemical reaction schemes. The left scheme shows the polymerization of monomer **46** to form polymer **48**. Monomer **46** is a ribose derivative with a base (B) at the C1 position, a substituent (X) at the C2 position, and a hydroxyl group at the C3 position. Polymer **48** is a linear polymer where the ribose units are linked via phosphorothioate groups, with the repeating unit shown in brackets with a subscript *n*. The right scheme shows the polymerization of monomer **44** with linker **35/36/37** to form polymer **50**. Monomer **44** is a ribose derivative with a base (B) at the C1 position, a substituent (X) at the C2 position, and a hydroxyl group at the C3 position. Linker **35/36/37** is a phosphorothioate group. Polymer **50** is a linear polymer where the ribose units are linked via phosphorothioate groups, with the repeating unit shown in brackets with a subscript *n*. The linker **35/36/37** is shown as a phosphorothioate group connecting the ribose units.

Figure 14

47
↓

45
+
32/33/34

↘

